# NMCP COVID-19 Literature Report #74: Friday, 13 August 2021

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**Purpose:** These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at https://nmcp.libguides.com/covidreport. Access is private; you will need to use the direct link or bookmark the URL.

**Disclaimer:** I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

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## The Big Picture

### *News in Brief*

*How It's Going (Spoiler: Not Great)*

04 August: "Global COVID-19 cases surpass 200 [million] as Delta variant spreads" (Reuters).

"Florida to receive hundreds of ventilators from U.S. government to help state's record hospitalizations" (WP).

Meanwhile, in Texas: "Texas hospital system is prepping tents to deal with rapid surge in Covid-19 patients" (CNN).

"For many, the belated realization that Covid will be 'a long war' sparks anger and denial" (STAT).

Opinion: "As bad as covid-19 has been, a future pandemic could be even worse — unless we act now" (WP).

*Long Reads*

Highly recommended: "How the pandemic now ends: Cases of COVID-19 are rising fast. Vaccine uptake has plateaued. The pandemic will be over one day—but the way there is different now" (Atlantic).

"Too many people are dying right now: 'It's hard to look at these indicators and feel at all optimistic,' explains scientist Eric Topol" (NY Mag; see also: twitter thread).

Perspective: "Assessing the threat of Covid 19-related extremism in the west" (ICCT).

### *Special Reports and Other Resources*

CRS: COVID-19: Potential Implications for International Security Environment—Overview of Issues and Further Reading for Congress [pdf] (05 August 2021)

> "Some observers argue the COVID-19 pandemic could be a world-changing event with potentially profound and long-lasting implications for the international security environment. Other observers are more skeptical that the pandemic will have such effects. This report provides a brief overview of some potential implications the pandemic might have for the international security environment, and appendices listing CRS reports and other writings for further reading.
>
> Issues for Congress may include whether and how the pandemic could change the international security environment, whether the Biden Administration's actions for responding to such change are appropriate and sufficient, and what implications such

> change could have for the role of Congress in setting and overseeing the execution of U.S. foreign and defense policy. Congress's decisions regarding these issues could have significant implications for U.S. foreign and defense policy.
>
> Appendix A presents a list of CRS reports that provide more in-depth discussions of issues presented in this report. Appendix B presents a list of additional writings reflecting various perspectives on these issues."

GAO: COVID-19: HHS's Collection of Hospital Capacity Data (05 August 2021)

> "In April 2020, Health and Human Services created a new data system to collect information on whether hospitals had enough beds and supplies during COVID.
>
> Throughout the pandemic, HHS changed its data collection methods and requirements, making it harder for some hospitals to report data.
>
> HHS used the data to distribute resources and inform the public. HHS officials said that some states that don't collect their own data also used it. Some public health organizations preferred to use more detailed state or local data for their purposes."

### *Upcoming Events*

TOPIC: Towards a Post-Pandemic World: Lessons from COVID-19 for Now and the Future, The National Academies of Sciences, Engineering, and Medicine (NASEM)

WHAT/WHEN: Free virtual workshop; 21-24 September 2021, 1000-1430 EDT

DETAILS: Join the Forum on Microbial Threats for an exciting virtual conversation about what we've learned from 15 months of living through a global pandemic. The workshop will broadly examine responses to COVID-19 in the U.S. and abroad, and will host retrospective and prospective discussions on the broad impacts of the pandemic on human health and society. Events will highlight successes, missed opportunities, and emerging data in order to extract key understandings that leaders in governments, public health systems, the private sector, and communities can incorporate into their ongoing pandemic responses now with a view towards enhancing resilience and preparedness for future outbreaks.

Individual workshop sessions will focus on:

- Anticipated long-term effects of COVID-19 (Day 1)
- Trust, engagement, and misinformation in public health (Day 2)
- Key questions on interventions and recovery from COVID-19 (Day 3)
- Building capacities for better pandemic preparedness and response (Day 4)

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For the agenda and more information, see: https://www.nationalacademies.org/event/07-27-2021/moving-past-covid-19-lessons-learned-from-responses-around-the-world

Register at: https://www.eventbrite.com/e/towards-a-post-pandemic-world-lessons-from-covid-19-for-now-and-the-future-tickets-159698413253

### *Journal Articles*

Clin Infect Dis: Leveraging a preexisting global infectious disease network for local decision-making during a pandemic (28 July 2021)

> "Emerging infectious disease epidemics require a rapid response from health systems; however, evidence-based consensus guidelines are generally absent early in the course of events. Formed in 2017 by five high-level isolation units spanning three continents, the experience of the Global Infectious Disease Preparedness Network (GIDPN) early in the course of COVID-19 provides a model for accelerating best practice development and improving decision-making in health emergencies. The network served as a platform for real-time, open and transparent information-sharing during unknowns of an active outbreak by clinicians caring for patients, by researchers conducting clinical trials and transmission and infection prevention studies, and by teams advising local and national policymakers. Shared knowledge led to earlier adoption of some treatment modalities as compared to most peer institutions and to implementation of protocols prior to incorporation into national guidelines. GIDPN and similar networks are integral in enhancing preparedness for and response to future epidemics/pandemics."

## SARS-CoV-2 Virus and Variants

### *News in Brief*

"Two-thirds of Americans in highly vaccinated counties now live in coronavirus hot spots, according to an analysis by The Washington Post" (WP).

"Vaccinated or not, most Virginians are projected to encounter coronavirus soon" (VP).

"Chinese state media has seized on a Swiss scientist critical of a covid origins probe. The one problem: He might not exist" (WP).

*Variants*

"Are COVID symptoms different with Delta? As reports of milder cold-like illness surface, experts suggest testing to know for sure" (Medpage).

"Remember Beta? New data reveal variant's deadly powers: People infected with a variant first identified in South Africa are more likely to die than those infected with other variants" (Nature).

There's some evidence that the spread of the Delta variant is associated with reduced vaccine effectiveness (medRxiv preprint).

"Here's what we know about the delta-plus variant" (WP).

"Unraveling the mysterious mutations that make delta the most transmissible Covid virus yet" (KHN).

*Long Reads*

"How will the coronavirus evolve? Delta won't be the last variant. What will the next ones bring?" (New Yorker).

### ***Journal Articles***

PNAS: Asymptomatic SARS-CoV-2 infection: A systematic review and meta-analysis (10 August 2021)

> "Quantification of asymptomatic infections is fundamental for effective public health responses to the COVID-19 pandemic. Discrepancies regarding the extent of asymptomaticity have arisen from inconsistent terminology as well as conflation of index and secondary cases which biases toward lower asymptomaticity. We searched PubMed, Embase, Web of Science, and World Health Organization Global Research Database on COVID-19 between January 1, 2020 and April 2, 2021 to identify studies that reported silent infections at the time of testing, whether presymptomatic or asymptomatic. Index cases were removed to minimize representational bias that would result in overestimation of symptomaticity. By analyzing over 350 studies, we estimate that the percentage of infections that never developed clinical symptoms, and thus were truly asymptomatic, was 35.1% (95% CI: 30.7 to 39.9%). At the time of testing, 42.8% (95% prediction interval: 5.2 to 91.1%) of cases exhibited no symptoms, a group comprising both asymptomatic and presymptomatic infections. Asymptomaticity was significantly lower among the elderly, at 19.7% (95% CI: 12.7 to 29.4%) compared with children at 46.7% (95% CI: 32.0 to 62.0%). We also found that cases with comorbidities had significantly lower asymptomaticity compared to cases with no underlying medical conditions. Without proactive policies to detect asymptomatic infections, such as rapid contact tracing, prolonged efforts for pandemic control may be needed even in the presence of vaccination."

MMWR: Rapid Increase in Circulation of the SARS-CoV-2 B.1.617.2 (Delta) Variant — Mesa County, Colorado, April–June 2021 (06 August 2021)

> "What is already known about this topic? The highly transmissible B.1.617.2 (Delta) variant of SARS-CoV-2 has become the predominant circulating U.S. strain.
>
> What is added by this report? During April–June 2021, COVID-19 cases caused by the Delta variant increased rapidly in Mesa County, Colorado. Compared with that in other Colorado counties, incidence, intensive care unit admissions, COVID-19 case fatality ratios, and the proportion of cases in fully vaccinated persons were significantly higher in Mesa County. Crude vaccine effectiveness against symptomatic infection was estimated to be 78% for Mesa County and 89% for other Colorado counties.
>
> What are the implications for public health practice? Vaccination is critical for preventing infection, serious illness, and death associated with SARS-CoV-2 infection (including the Delta variant). Multicomponent prevention strategies, such as masking in indoor settings irrespective of vaccination status as well as optimal surveillance testing and infection prevention and control, should be considered in areas of high incidence."

Nat Commun: Seven-month kinetics of SARS-CoV-2 antibodies and role of pre-existing antibodies to human coronaviruses (06 August 2021)

> "Unraveling the long-term kinetics of antibodies to SARS-CoV-2 and the individual characteristics influencing it, including the impact of pre-existing antibodies to human coronaviruses causing common cold (HCoVs), is essential to understand protective immunity to COVID-19 and devise effective surveillance strategies. IgM, IgA and IgG levels against six SARS-CoV-2 antigens and the nucleocapsid antigen of the four HCoV (229E, NL63, OC43 and HKU1) were quantified by Luminex, and antibody neutralization capacity was assessed by flow cytometry, in a cohort of health care workers followed up to 7 months (N = 578). Seroprevalence increases over time from 13.5% (month 0) and 15.6% (month 1) to 16.4% (month 6). Levels of antibodies, including those with neutralizing capacity, are stable over time, except IgG to nucleocapsid antigen and IgM levels that wane. After the peak response, anti-spike antibody levels increase from ~150 days post-symptom onset in all individuals (73% for IgG), in the absence of any evidence of re-exposure. IgG and IgA to HCoV are significantly higher in asymptomatic than symptomatic seropositive individuals. Thus, pre-existing cross-reactive HCoVs antibodies could have a protective effect against SARS-CoV-2 infection and COVID-19 disease."

## COVID-19 Vaccines

### *News in Brief*

"FDA, under pressure, plans 'sprint' to accelerate review of Pfizer's Covid-19 vaccine for full approval" (STAT).

The FDA has updated the EUAs for Pfizer and Moderna COVID-19 vaccines to allow a third booster dose for certain immunocompromised people (Medpage; see also: FDA news release).

*Vaccine Access*

"Alabama just tossed 65,000 vaccines. Turns out it's not easy to donate unused doses" (NPR).

"A snort or a jab? Scientists debate potential benefits of intranasal Covid-19 vaccines" (STAT).

*Vaccine Effectiveness*

"How do vaccinated people spread Delta? What the science says: Emerging data suggest that Delta could spread more readily than other coronavirus variants among people vaccinated against COVID-19. But key questions remain" (Nature).

"They worry the Johnson & Johnson shot isn't enough. A new study offers answers — and questions" (WP).

"Moderna's COVID-19 vaccine appeared to have a higher effectiveness rate compared with the Pfizer vaccine during the period of time when the Delta variant first became predominant" (Medpage; see also: medRxiv preprint).

*Vaccine Development*

"The COVID vaccine makers tell all: A book from the Oxford–AstraZeneca team, and a documentary, go behind the scenes in the race to vaccinate the world" (Nature).

Fun fact: Sarah Gilbert, one of the scientists behind the AstraZeneca vaccine (and co-author of the aforementioned book), is getting made into a Barbie doll (NPR).

### *Special Reports and Other Resources*

CRS: Defense Health Primer: Military Vaccinations [pdf] (06 August 2021)

> "This In Focus describes DOD's military vaccination policies and immunization program, and offers issues for congressional consideration."

### *Journal Articles*

NEJM: Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant (12 August 2021)

> "The B.1.617.2 (delta) variant of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (Covid-19), has contributed to a surge in cases in India and has now been detected across the globe, including a notable increase in cases in the United Kingdom. The effectiveness of the BNT162b2 and ChAdOx1 nCoV-19 vaccines against this variant has been unclear.
>
> We used a test-negative case–control design to estimate the effectiveness of vaccination against symptomatic disease caused by the delta variant or the predominant strain (B.1.1.7, or alpha variant) over the period that the delta variant began circulating. Variants were identified with the use of sequencing and on the basis of the spike (S) gene status. Data on all symptomatic sequenced cases of Covid-19 in England were used to estimate the proportion of cases with either variant according to the patients' vaccination status.
>
> Effectiveness after one dose of vaccine (BNT162b2 or ChAdOx1 nCoV-19) was notably lower among persons with the delta variant (30.7%; 95% confidence interval [CI], 25.2 to 35.7) than among those with the alpha variant (48.7%; 95% CI, 45.5 to 51.7); the results were similar for both vaccines. With the BNT162b2 vaccine, the effectiveness of two doses was 93.7% (95% CI, 91.6 to 95.3) among persons with the alpha variant and 88.0% (95% CI, 85.3 to 90.1) among those with the delta variant. With the ChAdOx1 nCoV-19 vaccine, the effectiveness of two doses was 74.5% (95% CI, 68.4 to 79.4) among persons with the alpha variant and 67.0% (95% CI, 61.3 to 71.8) among those with the delta variant.
>
> Only modest differences in vaccine effectiveness were noted with the delta variant as compared with the alpha variant after the receipt of two vaccine doses. Absolute differences in vaccine effectiveness were more marked after the receipt of the first dose. This finding would support efforts to maximize vaccine uptake with two doses among vulnerable populations."

Clin Infect Dis: Determining the Incidence of Asymptomatic SARS-CoV-2 among Early Recipients of COVID-19 Vaccines: A Prospective Cohort Study of Healthcare Workers before, during and after Vaccination [DISCOVER-COVID-19] (07 August 2021)

> "The impact of COVID19 vaccination on viral characteristics of breakthrough infections is unknown. In this prospective cohort study, incidence of SARS-CoV-2 infection decreased following vaccination. Although asymptomatic positive tests were observed following vaccination, higher cycle thresholds, repeat negative tests and inability to culture virus raises questions about their clinical significance."

*Preventing Hospitalization*

MMWR: Effectiveness of COVID-19 Vaccines in Preventing Hospitalization Among Adults Aged ≥65 Years — COVID-NET, 13 States, February–April 2021 (06 August 2021)

> "What is already known about this topic? Clinical trials of COVID-19 vaccines currently authorized for emergency use in the United States (Pfizer-BioNTech, Moderna, and Janssen [Johnson & Johnson]) have shown high efficacy in preventing symptomatic (including moderate to severe) COVID-19.
>
> What is added by this report? Among adults aged 65–74 years, effectiveness of full vaccination for preventing hospitalization was 96% for Pfizer-BioNTech, 96% for Moderna, and 84% for Janssen COVID-19 vaccines; among adults aged ≥75 years, effectiveness of full vaccination for preventing hospitalization was 91% for Pfizer-BioNTech, 96% for Moderna, and 85% for Janssen COVID-19 vaccines.
>
> What are the implications for public health practice? Efforts to increase vaccination coverage are critical to reducing the risk for COVID-19–related hospitalization, particularly in older adults."

Clin Infect Dis: Effectiveness of SARS-CoV-2 mRNA Vaccines for Preventing Covid-19 Hospitalizations in the United States (06 August 2021)

> "Background: As SARS-CoV-2 vaccination coverage increases in the United States (US), there is a need to understand the real-world effectiveness against severe Covid-19 and among people at increased risk for poor outcomes.
>
> Methods: In a multicenter case-control analysis of US adults hospitalized March 11-May 5, 2021, we evaluated vaccine effectiveness to prevent Covid-19 hospitalizations by comparing odds of prior vaccination with an mRNA vaccine (Pfizer-BioNTech or Moderna) between cases hospitalized with Covid-19 and hospital-based controls who tested negative for SARS-CoV-2.
>
> Results: Among 1212 participants, including 593 cases and 619 controls, median age was 58 years, 22.8% were Black, 13.9% were Hispanic, and 21.0% had immunosuppression. SARS-CoV-2 lineage B.1.1.7 (Alpha) was the most common variant (67.9% of viruses with lineage determined). Full vaccination (receipt of two vaccine doses ≥14 days before illness onset) had been received by 8.2% of cases and 36.4% of controls. Overall vaccine effectiveness was 87.1% (95% CI: 80.7 to 91.3%).
>
> Vaccine effectiveness was similar for Pfizer-BioNTech and Moderna vaccines, and highest in adults aged 18-49 years (97.4%; 95% CI: 79.3 to 99.7%). Among 45 patients with vaccine-breakthrough Covid hospitalizations, 44 (97.8%) were ≥50 years old and 20 (44.4%) had immunosuppression. Vaccine effectiveness was lower among patients with

> immunosuppression (62.9%; 95% CI: 20.8 to 82.6%) than without immunosuppression (91.3%; 95% CI: 85.6 to 94.8%).
>
> Conclusion: During March-May 2021, SARS-CoV-2 mRNA vaccines were highly effective for preventing Covid-19 hospitalizations among US adults. SARS-CoV-2 vaccination was beneficial for patients with immunosuppression, but effectiveness was lower in the immunosuppressed population."

### *Vaccines in Cancer Patients*

JAMA Oncol: Antibody Response to COVID-19 Vaccination in Adults With Hematologic Malignant Disease (11 August 2021)

> "This retrospective case series study examines immune response of adults with hematologic malignant disease who were vaccinated with 1 of 3 FDA-authorized COVID-19 vaccines between February and April of 2021….
>
> Longer time from last chemotherapy administration to vaccination was associated with increased rates of seroconversion (median 8.4 vs 0 months, P = .005). Among patients who completed chemotherapy longer than 12 months before vaccination (n = 32), 69% showed seroconversion, compared with 24% among those who were vaccinated within 12 months of last treatment (n = 97)…. Three patients developed COVID-19 infections after vaccination (with no detectable post-vaccination antibodies) with 1 death."

JAMA Oncol: Durability of Response to SARS-CoV-2 BNT162b2 Vaccination in Patients on Active Anticancer Treatment (11 August 2021)

> "This cohort study examines the durability of immune response from BNT162b2 vaccination for severe acute respiratory syndrome coronavirus 2 in patients with cancer vs healthy controls….
>
> The seropositivity rate among the patients with cancer remained high (87%) approximately 4 months after the second BNT162b2 vaccination dose. The median IgG titer in the patients and the controls decreased over time."

### *Adverse Effects: General*

JAMA Cardiol: Clinical Characteristics and Pharmacological Management of COVID-19 Vaccine–Induced Immune Thrombotic Thrombocytopenia With Cerebral Venous Sinus Thrombosis: A Review (10 August 2021)

> "Importance The COVID-19 pandemic saw one of the fastest developments of vaccines in an effort to combat an out-of-control pandemic. The 2 most common COVID-19 vaccine platforms currently in use, messenger RNA (mRNA) and adenovirus vector, were developed on the basis of previous research in use of this technology. Postauthorization surveillance of COVID-19 vaccines has identified safety signals, including unusual cases of thrombocytopenia with thrombosis reported in recipients of adenoviral vector vaccines. One of the devastating manifestations of this syndrome, termed vaccine-induced immune thrombotic thrombocytopenia (VITT), is cerebral venous sinus thrombosis (CVST). This review summarizes the current evidence and indications regarding biology, clinical characteristics, and pharmacological management of VITT with CVST.
>
> Observations VITT appears to be similar to heparin-induced thrombocytopenia (HIT), with both disorders associated with thrombocytopenia, thrombosis, and presence of autoantibodies to platelet factor 4 (PF4). Unlike VITT, HIT is triggered by recent exposure to heparin. Owing to similarities between these 2 conditions and lack of high-quality evidence, interim recommendations suggest avoiding heparin and heparin analogues in patients with VITT. Based on initial reports, female sex and age younger than 60 years were identified as possible risk factors for VITT.
>
> Treatment consists of therapeutic anticoagulation with nonheparin anticoagulants and prevention of formation of autoantibody-PF4 complexes, the latter being achieved by administration of high-dose intravenous immunoglobin (IVIG). Steroids, which can theoretically inhibit the production of new antibodies, have been used in combination with IVIG. In severe cases, plasma exchange should be used for clearing autoantibodies. Monoclonal antibodies, such as rituximab and eculizumab, can be considered when other therapies fail. Routine platelet transfusions, aspirin, and warfarin should be avoided because of the possibility of worsening thrombosis and magnifying bleeding risk.
>
> Conclusions and Relevance Adverse events like VITT, while uncommon, have been described despite vaccination remaining the most essential component in the fight against the COVID-19 pandemic. While it seems logical to consider the use of types of vaccines (eg, mRNA-based administration) in individuals at high risk, treatment should consist of therapeutic anticoagulation mostly with nonheparin products and IVIG."

MMWR: Use of COVID-19 Vaccines After Reports of Adverse Events Among Adult Recipients of Janssen (Johnson & Johnson) and mRNA COVID-19 Vaccines (Pfizer-BioNTech and Moderna): Update from the Advisory Committee on Immunization Practices — United States, July 2021 (10 August 2021)

> "What is already known about this topic? Rare serious adverse events have been reported after COVID-19 vaccination, including Guillain-Barré syndrome (GBS) and thrombosis with

> thrombocytopenia syndrome (TTS) after Janssen COVID-19 vaccination and myocarditis after mRNA (Pfizer-BioNTech and Moderna) COVID-19 vaccination.
>
> What is added by this report? On July 22, 2021, the Advisory Committee on Immunization Practices reviewed updated benefit-risk analyses after Janssen and mRNA COVID-19 vaccination and concluded that the benefits outweigh the risks for rare serious adverse events after COVID-19 vaccination.
>
> What are the implications for public health practice? Continued COVID-19 vaccination will prevent COVID-19 morbidity and mortality far exceeding GBS, TTS, and myocarditis cases expected. Information about rare adverse events should be disseminated to providers, vaccine recipients, and the public."

*Adverse Effects: Myocarditis*

JAMA Cardiol: Association of Myocarditis With BNT162b2 Messenger RNA COVID-19 Vaccine in a Case Series of Children (10 August 2021)

> "Question  What are the findings on cardiac imaging in children with myocarditis after COVID-19 vaccination?
>
> Findings  In this case series of 15 children who were hospitalized with myocarditis after receipt of the BNT162b2 messenger RNA COVID-19 vaccine for 1 to 5 days, boys were most often affected after the second vaccine dose, 3 patients had ventricular systolic dysfunction, and 12 patients had late gadolinium enhancement on cardiac magnetic resonance imaging. There was no mortality, and all but 1 patient had normal echocardiogram results on follow-up 1 to 13 days after discharge.
>
> Meaning  COVID-19 vaccine-associated myocarditis may have a benign short-term course in children; however, the long-term risks remain unknown."

JAMA: Myocarditis and Pericarditis After Vaccination for COVID-19 (04 August 2021)

> "This study investigates the incidence of myocarditis and pericarditis emergency department or inpatient hospital encounters before COVID-19 vaccine availability (January 2019–January 2021) and during a COVID-19 vaccination period (February-May 2021) in a large US health care system….
>
> Two distinct self-limited syndromes, myocarditis and pericarditis, were observed after COVID-19 vaccination. Myocarditis developed rapidly in younger patients, mostly after the second vaccination. Pericarditis affected older patients later, after either the first or second dose."

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## Vaccine Hesitancy, Vaccine Denial, and Health Misinformation

### *News in Brief*

"My brother is one of millions who won't get the COVID-19 vaccine. I asked why. Here are his reasons, my responses" (USA Today).

"A WHO official on why we need a global tech strategy to fight vaccine misinformation" (STAT).

"NYU researchers were studying disinformation on Facebook. The company cut them off" (NPR).

The *Journal of Medical Internet Research* has put out a call for papers to a special theme issue "examining the intersection of social media, ethics, and COVID-19 misinformation". For more information, see: https://www.jmir.org/announcements/275

### *Journal Articles*

Nature: Behavioral Nudges Increase COVID-19 Vaccinations (02 August 2021)

> "Enhancing vaccine uptake is a critical public health challenge. Overcoming vaccine hesitancy and failure to follow-through on vaccination intentions requires effective communication strategies. We present two sequential randomized controlled trials (RCTs) to test the impact of behavioral interventions on COVID-19 vaccine uptake. We designed text-based reminders that make vaccination salient and easy, and delivered them to patients of a healthcare system one day (first RCT; N=93,354, clinicaltrials #NCT04800965) and eight days (second RCT; N=67,092, NCT04801524) after they received notification of vaccine eligibility.
>
> The first reminder boosted appointments and vaccination rates within the healthcare system by 6.07 (84%) and 3.57 (26%) percentage points, respectively; the second reminder increased those outcomes by 1.65 and 1.06 percentage points, respectively. The first reminder was more impactful when it made patients feel the vaccine was already theirs. However, we find no evidence that combining it with an information intervention addressing vaccine hesitancy heightened its effect. Online studies (N=3,181) examining vaccination intentions reveal divergent patterns from the first RCT, underscoring the importance of pilot-testing interventions in the field. These findings inform the design of behavioral nudges for promoting health decisions, highlighting the value of making vaccination easy and inducing feelings of ownership."

## Breakthrough Infections, Reinfections, and Coinfections

### *News in Brief*

"Breakthrough COVID-19 infection risk may differ with vaccine type, early Mayo Clinic research suggests" (BHR; see also: medRxiv preprint).

### *Journal Articles*

Clin Infect Dis: The Impact of COVID-19 on Healthcare-Associated Infections (09 August 2021)

> "Background: The profound changes wrought by COVID-19 on routine hospital operations may have influenced performance on hospital measures, including healthcare-associated infections (HAIs). We aimed to evaluate the association between COVID-19 surges and HAI and cluster rates.
>
> Methods: In 148 HCA Healthcare-affiliated hospitals, 3/1/2020-9/30/2020, and a subset of hospitals with microbiology and cluster data through 12/31/2020, we evaluated the association between COVID-19 surges and HAIs, hospital-onset pathogens, and cluster rates using negative binomial mixed models. To account for local variation in COVID-19 pandemic surge timing, we included the number of discharges with a laboratory-confirmed COVID-19 diagnosis per staffed bed per month.
>
> Results: Central line-associated blood stream infections (CLABSI), catheter-associated urinary tract infections (CAUTI), and methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia increased as COVID-19 burden increased. There were 60% (95% CI, 23-108%) more CLABSI, 43% (95% CI, 8-90%) more CAUTI, and 44% (95% CI, 10-88%) more cases of MRSA bacteremia than expected over 7 months based on predicted HAIs had there not been COVID-19 cases. *Clostridioides difficile* infection was not significantly associated with COVID-19 burden. Microbiology data from 81 of the hospitals corroborated the findings.
>
> Notably, rates of hospital-onset bloodstream infections and multidrug resistant organisms, including MRSA, vancomycin-resistant enterococcus and Gram-negative organisms were each significantly associated with COVID-19 surges. Finally, clusters of hospital-onset pathogens increased as the COVID-19 burden increased.
>
> Conclusion: COVID-19 surges adversely impact HAI rates and clusters of infections within hospitals, emphasizing the need for balancing COVID-related demands with routine hospital infection prevention."

MMWR: Reduced Risk of Reinfection with SARS-CoV-2 After COVID-19 Vaccination — Kentucky, May–June 2021 (06 August 2021)

> "What is already known about this topic? Reinfection with human coronaviruses, including SARS-CoV-2, the virus that causes COVID-19, has been documented. Currently, limited evidence concerning the protection afforded by vaccination against reinfection with SARS-CoV-2 is available.
>
> What is added by this report? Among Kentucky residents infected with SARS-CoV-2 in 2020, vaccination status of those reinfected during May–June 2021 was compared with that of residents who were not reinfected. In this case-control study, being unvaccinated was associated with 2.34 times the odds of reinfection compared with being fully vaccinated.
>
> What are the implications for public health practice? To reduce their likelihood for future infection, all eligible persons should be offered COVID-19 vaccine, even those with previous SARS-CoV-2 infection."

Clin Infect Dis: Suspected SARS-CoV-2 Reinfections: Incidence, Predictors, and Healthcare Use among Patients at 238 U.S. Healthcare Facilities, June 1, 2020- February 28, 2021 (05 August 2021)

> "In a retrospective cohort study, among 131,773 patients with previous COVID19, reinfection with SARS-CoV-2 was suspected in 253(0.2%) patients at 238 U.S. healthcare facilities between June 1, 2020- February 28, 2021. Women displayed a higher cumulative reinfection risk. Healthcare burden and illness severity were similar between index and reinfection encounters."

Infect Control Hosp Epidemiol: Risk Factors and Outcomes Associated with Community-Onset and Hospital-Acquired Co-infection in Patients Hospitalized for COVID-19: A Multi-Hospital Cohort Study (26 July 2021)

> "Background: We sought to determine the incidence of community-onset and hospital-acquired co-infection in patients hospitalized with COVID-19 and evaluate associated predictors and outcomes.
>
> Methods: Multicenter retrospective cohort study of patients hospitalized for COVID-19, 3/2020 to 8/2020, across 38 Michigan hospitals assessed for prevalence, predictors, and outcomes of community-onset or hospital-acquired co-infection. In-hospital and 60-day mortality, readmission, discharge to long-term care facility (LTCF), and mechanical ventilation duration, were assessed for patients with vs. without co-infection.
>
> Results: Of 2205 patients with COVID-19, 6.4% (N=141) had a co-infection (3.0% community-onset, 3.4% hospital-acquired). 64.9% of patients without co-infection received antibiotics. Community-onset co-infection predictors include admission from LTCF (OR 3.98,

> 95% CI 2.34-6.76, p<0.001) and admission to intensive care (OR 4.34, 95% CI 2.87-6.55, p<0.001). Hospital-acquired co-infection predictors include fever (OR 2.46, 95% CI 1.15-5.27, p=0.02) and advanced respiratory support (OR 40.72, 95% CI 13.49-122.93, p<0.001). Patients with (vs. without) community-onset co-infection had longer mechanical ventilation (OR 3.31, 95% CI 1.67-6.56, p=0.001) and higher in-hospital (OR 1.90, 95% CI 1.06-3.40 p=0.03) and 60-day mortality (OR 1.86, 95% CI 1.05-3.29 p=0.03). Patients with (vs. without) hospital-acquired co-infection had higher discharge to LTCF (OR 8.48, 95%CI 3.30-21.76 p<0.001), in-hospital (OR 4.17, 95% CI 2.37-7.33, p=<.001) and 60-day mortality (OR 3.66, 95% CI 2.11-6.33, p=<.001).
>
> Conclusion: Despite community-onset and hospital-acquired co-infection being uncommon, most patients hospitalized with COVID-19 received antibiotics. Admission from LTCF and to ICU were associated with increased risk of community-onset co-infection. Future work should prospectively validate predictors of COVID-19 co-infection to facilitate antibiotic reduction."

## Treatments and Management

### *News in Brief*

04 August: NIH updated treatment guidelines on anti-SARS-CoV-2 monoclonal antibodies; see: https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/whats-new/

ICYMI: A recording of the webinar "Therapeutic Options to Prevent Severe COVID-19 in Immunocompromised People" is now available (CDC).

*Clinical Trials*

The ACTIV-6 trial will now include home-based treatments for mild-to-moderate COVID-19 (DCRI).

WHO's Solidarity trial is expanding to test artesunate, imatinib and infliximab for hospitalized COVID-19 patients across 52 countries (WHO; see also: trial registry).

*State of the Literature*

A meta-analysis of ivermectin for treatment of SARS-CoV-2 infection published last month in *Open Forum Infectious Diseases* (and noted in COVID lit report #72) has had an expression of concern, leading the authors to retract and revise the paper (RW).

### *Journal Articles*

Clin Infect Dis: SARS-CoV-2 Viremia is Associated with COVID-19 Severity and Predicts Clinical Outcomes (10 August 2021)

> "Background: SARS-CoV-2 viral RNA (vRNA) is detected in the bloodstream of some patients with COVID-19 ("RNAemia") but it is not clear whether this RNAemia reflects viremia (i.e., virus particles) and how RNAemia/viremia is related to host immune responses and outcomes.
>
> Methods: SARS-CoV-2 vRNA was quantified by ultra-sensitive RT-PCR in plasma samples (0.5-1.0 ml) from observational cohorts of 51 COVID-19 patients including 9 outpatients, 19 hospitalized (non-ICU), and 23 ICU patients, and vRNA levels compared with cross-sectional indices of COVID-19 severity and prospective clinical outcomes. We used multiple imaging methods to visualize virions in pelleted plasma.
>
> Results: SARS-CoV-2 vRNA was detected in plasma of 100%, 52.6% and 11.1% of ICU, non-ICU, and outpatients respectively. Virions were detected in plasma pellets by electron tomography and immunostaining. Plasma vRNA levels were significantly higher in ICU > non-ICU > outpatients (p<0.0001); and for inpatient, plasma vRNA levels were strongly associated with higher WHO score at admission (p=0.01), maximum WHO score (p=0.002) and discharge disposition (p=0.004). A plasma vRNA level >6,000 copies/ml was strongly associated with mortality (HR: 10.7). Levels of vRNA were significantly associated with several inflammatory biomarkers (p<0.01) but not with plasma neutralizing antibody titers (p=0.8).
>
> Conclusions: Visualization of virus particles in plasma indicates that SARS-CoV-2 RNAemia is due, at least in part, to viremia. The levels of SARS-CoV-2 RNAemia quantified by ultrasensitive RT-PCR correlate strongly with disease severity, patient outcome and specific inflammatory biomarkers but not neutralizing antibody titers."

Lancet: Inhaled budesonide for COVID-19 in people at high risk of complications in the community in the UK (PRINCIPLE): a randomised, controlled, open-label, adaptive platform trial (10 August 2021)

> "A previous efficacy trial found benefit from inhaled budesonide for COVID-19 in patients not admitted to hospital, but effectiveness in high-risk individuals is unknown. We aimed to establish whether inhaled budesonide reduces time to recovery and COVID-19-related hospital admissions or deaths among people at high risk of complications in the community.
>
> PRINCIPLE is a multicentre, open-label, multi-arm, randomised, controlled, adaptive platform trial done remotely from a central trial site and at primary care centres in the UK. Eligible participants were aged 65 years or older or 50 years or older with comorbidities, and unwell for up to 14 days with suspected COVID-19 but not admitted to hospital.

> Participants were randomly assigned to usual care, usual care plus inhaled budesonide (800 µg twice daily for 14 days), or usual care plus other interventions, and followed up for 28 days. Participants were aware of group assignment. The coprimary endpoints are time to first self-reported recovery and hospital admission or death related to COVID-19, within 28 days, analysed using Bayesian models. The primary analysis population included all eligible SARS-CoV-2-positive participants randomly assigned to budesonide, usual care, and other interventions, from the start of the platform trial until the budesonide group was closed. This trial is registered at the ISRCTN registry (ISRCTN86534580) and is ongoing.
>
> The trial began enrolment on April 2, 2020, with randomisation to budesonide from Nov 27, 2020, until March 31, 2021, when the prespecified time to recovery superiority criterion was met. 4700 participants were randomly assigned to budesonide (n=1073), usual care alone (n=1988), or other treatments (n=1639). The primary analysis model includes 2530 SARS-CoV-2-positive participants, with 787 in the budesonide group, 1069 in the usual care group, and 974 receiving other treatments.
>
> There was a benefit in time to first self-reported recovery of an estimated 2·94 days (95% Bayesian credible interval [BCI] 1·19 to 5·12) in the budesonide group versus the usual care group (11·8 days [95% BCI 10·0 to 14·1] vs 14·7 days [12·3 to 18·0]; hazard ratio 1·21 [95% BCI 1·08 to 1·36]), with a probability of superiority greater than 0·999, meeting the prespecified superiority threshold of 0·99. For the hospital admission or death outcome, the estimated rate was 6·8% (95% BCI 4·1 to 10·2) in the budesonide group versus 8·8% (5·5 to 12·7) in the usual care group (estimated absolute difference 2·0% [95% BCI –0·2 to 4·5]; odds ratio 0·75 [95% BCI 0·55 to 1·03]), with a probability of superiority 0·963, below the prespecified superiority threshold of 0·975. Two participants in the budesonide group and four in the usual care group had serious adverse events (hospital admissions unrelated to COVID-19).
>
> Inhaled budesonide improves time to recovery, with a chance of also reducing hospital admissions or deaths (although our results did not meet the superiority threshold), in people with COVID-19 in the community who are at higher risk of complications."

Infect Control Hosp Epidemiol: Antimicrobial Stewardship in Patients with Confirmed COVID-19 (02 August 2021)

> "173 hospitalized COVID-19 patients receiving antibiotics were retrospectively assigned to the early or late discontinuation groups. Length of therapy was shorter in the early discontinuation group (3 vs 7 days, p<0.0001). Mortality (14.3% vs 20.7%, p=0.316) and length of stay (7 vs. 9 days, p=0.063) were similar."

### *Anticoagulation*

NEJM: Therapeutic Anticoagulation with Heparin in Noncritically Ill Patients with Covid-19 (04 August 2021)

> "Background: Thrombosis and inflammation may contribute to the risk of death and complications among patients with coronavirus disease 2019 (Covid-19). We hypothesized that therapeutic-dose anticoagulation may improve outcomes in noncritically ill patients who are hospitalized with Covid-19.
>
> Methods: In this open-label, adaptive, multiplatform, controlled trial, we randomly assigned patients who were hospitalized with Covid-19 and who were not critically ill (which was defined as an absence of critical care-level organ support at enrollment) to receive pragmatically defined regimens of either therapeutic-dose anticoagulation with heparin or usual-care pharmacologic thromboprophylaxis. The primary outcome was organ support-free days, evaluated on an ordinal scale that combined in-hospital death (assigned a value of -1) and the number of days free of cardiovascular or respiratory organ support up to day 21 among patients who survived to hospital discharge. This outcome was evaluated with the use of a Bayesian statistical model for all patients and according to the baseline d-dimer level.
>
> Results: The trial was stopped when prespecified criteria for the superiority of therapeutic-dose anticoagulation were met. Among 2219 patients in the final analysis, the probability that therapeutic-dose anticoagulation increased organ support-free days as compared with usual-care thromboprophylaxis was 98.6% (adjusted odds ratio, 1.27; 95% credible interval, 1.03 to 1.58). The adjusted absolute between-group difference in survival until hospital discharge without organ support favoring therapeutic-dose anticoagulation was 4.0 percentage points (95% credible interval, 0.5 to 7.2). The final probability of the superiority of therapeutic-dose anticoagulation over usual-care thromboprophylaxis was 97.3% in the high d-dimer cohort, 92.9% in the low d-dimer cohort, and 97.3% in the unknown d-dimer cohort. Major bleeding occurred in 1.9% of the patients receiving therapeutic-dose anticoagulation and in 0.9% of those receiving thromboprophylaxis.
>
> Conclusions: In noncritically ill patients with Covid-19, an initial strategy of therapeutic-dose anticoagulation with heparin increased the probability of survival to hospital discharge with reduced use of cardiovascular or respiratory organ support as compared with usual-care thromboprophylaxis."

NEJM: Therapeutic Anticoagulation with Heparin in Critically Ill Patients with Covid-19 (04 August 2021)

> "Background: Thrombosis and inflammation may contribute to morbidity and mortality among patients with coronavirus disease 2019 (Covid-19). We hypothesized that

> therapeutic-dose anticoagulation would improve outcomes in critically ill patients with Covid-19.
>
> Methods: In an open-label, adaptive, multiplatform, randomized clinical trial, critically ill patients with severe Covid-19 were randomly assigned to a pragmatically defined regimen of either therapeutic-dose anticoagulation with heparin or pharmacologic thromboprophylaxis in accordance with local usual care. The primary outcome was organ support-free days, evaluated on an ordinal scale that combined in-hospital death (assigned a value of -1) and the number of days free of cardiovascular or respiratory organ support up to day 21 among patients who survived to hospital discharge.
>
> Results: The trial was stopped when the prespecified criterion for futility was met for therapeutic-dose anticoagulation. Data on the primary outcome were available for 1098 patients (534 assigned to therapeutic-dose anticoagulation and 564 assigned to usual-care thromboprophylaxis). The median value for organ support-free days was 1 (interquartile range, -1 to 16) among the patients assigned to therapeutic-dose anticoagulation and was 4 (interquartile range, -1 to 16) among the patients assigned to usual-care thromboprophylaxis (adjusted proportional odds ratio, 0.83; 95% credible interval, 0.67 to 1.03; posterior probability of futility [defined as an odds ratio <1.2], 99.9%). The percentage of patients who survived to hospital discharge was similar in the two groups (62.7% and 64.5%, respectively; adjusted odds ratio, 0.84; 95% credible interval, 0.64 to 1.11). Major bleeding occurred in 3.8% of the patients assigned to therapeutic-dose anticoagulation and in 2.3% of those assigned to usual-care pharmacologic thromboprophylaxis.
>
> Conclusions: In critically ill patients with Covid-19, an initial strategy of therapeutic-dose anticoagulation with heparin did not result in a greater probability of survival to hospital discharge or a greater number of days free of cardiovascular or respiratory organ support than did usual-care pharmacologic thromboprophylaxis."

## Pre-Existing Conditions, Comorbidities, and Impact on Other Diseases

### *Journal Articles*

EClinicalMedicine: Antiphospholipid antibodies and neurological manifestations in acute COVID-19: A single-centre cross-sectional study (12 August 2021)

> "A high prevalence of antiphospholipid antibodies has been reported in case series of patients with neurological manifestations and COVID-19; however, the pathogenicity of antiphospholipid antibodies in COVID-19 neurology remains unclear.

> This single-centre cross-sectional study included 106 adult patients: 30 hospitalised COVID-neurological cases, 47 non-neurological COVID-hospitalised controls, and 29 COVID-non-hospitalised controls, recruited between March and July 2020. We evaluated nine antiphospholipid antibodies: anticardiolipin antibodies [aCL] IgA, IgM, IgG; anti-beta-2 glycoprotein-1 [aβ2GPI] IgA, IgM, IgG; anti-phosphatidylserine/prothrombin [aPS/PT] IgM, IgG; and anti-domain I β2GPI (aD1β2GPI) IgG.
>
> There was a high prevalence of antiphospholipid antibodies in the COVID-neurological (73.3%) and non-neurological COVID-hospitalised controls (76.6%) in contrast to the COVID-non-hospitalised controls (48.2%). aPS/PT IgG titres were significantly higher in the COVID-neurological group compared to both control groups ($p < 0.001$). Moderate-high titre of aPS/PT IgG was found in 2 out of 3 (67%) patients with acute disseminated encephalomyelitis [ADEM]. aPS/PT IgG titres negatively correlated with oxygen requirement ($FiO_2$ $R=-0.15$ $p = 0.040$) and was associated with venous thromboembolism ($p = 0.043$). In contrast, aCL IgA ($p < 0.001$) and IgG ($p < 0.001$) was associated with non-neurological COVID-hospitalised controls compared to the other groups and correlated positively with d-dimer and creatinine but negatively with FiO2.
>
> Our findings show that aPS/PT IgG is associated with COVID-19-associated ADEM. In contrast, aCL IgA and IgG are seen much more frequently in non-neurological hospitalised patients with COVID-19. Characterisation of antiphospholipid antibody persistence and potential longitudinal clinical impact are required to guide appropriate management."

NEJM: SARS-CoV-2 Variants in Patients with Immunosuppression (05 August 2021)

> "In this article, the authors discuss the challenges of SARS-CoV-2 infection in patients with a weakened immune system, including the potential implications regarding viral evolution and transmission."

JAMA Netw Open: Factors Associated With Use of and Satisfaction With Telehealth by Adults in Rural Virginia During the COVID-19 Pandemic (02 August 2021)

> "This survey study examines the use of and satisfaction with telehealth services by adults in rural Virginia during the COVID-19 pandemic….
>
> Utilization of and satisfaction with telehealth services in this sample were associated with regular internet access, higher health literacy, and greater perceived stress. Demographic variables were not significantly associated with use of telehealth."

J Infect Dis: Clinical, immunological and virological SARS-CoV-2 phenotypes in obese and non-obese military health system beneficiaries (31 July 2021)

> "Background: The mechanisms underlying the association between obesity and COVID-19 severity remain unclear. After verifying that obesity was a correlate of severe COVID-19 in

> U.S. Military Health System (MHS) beneficiaries, we compared immunological and virological phenotypes of SARS-CoV-2 infection in both obese and non-obese participants.
>
> Methods: COVID-19-infected MHS beneficiaries were enrolled, and anthropometric, clinical, and demographic data were collected. We compared the SARS-CoV-2 peak IgG humoral response and RT-PCR viral load in obese and non-obese patients, stratified by hospitalization, utilizing logistic regression models.
>
> Results: 511 COVID-19 patients were analyzed, among whom 24% were obese and 14% severely-obese. Obesity was independently associated with hospitalization (aOR = 1.91, 95% CI = 1.15-3.18) and need for oxygen therapy (aOR = 3.39, 95% CI = 1.61-7.11). In outpatients, severely-obese had a log10 (1.89) higher N1 genome equivalents (GE)/reaction and log10 (2.62) higher N2 GE/reaction than non-obese ($p = 0.03$ and $p < 0.001$, respectively). We noted a correlation between BMI and peak anti-spike protein IgG in inpatients and outpatients (coefficient = 5.48, $p < 0.001$).
>
> Conclusions: Obesity is a strong correlate of COVID-19 severity in MHS beneficiaries. These findings offer new pathophysiological insights into the relationship between obesity and COVID-19 severity."

### *Hospital-Acquired Infections*

Emerg Infect Dis: Bloodstream Infection Risk, Incidence, and Deaths for Hospitalized Patients during Coronavirus Disease Pandemic (05 August 2021)

> "Hospital-acquired infections are emerging major concurrent conditions during the coronavirus disease (COVID-19) pandemic. We conducted a retrospective review of hospitalizations during March–October 2020 of adults tested by reverse transcription PCR for severe acute respiratory syndrome coronavirus 2. We evaluated associations of COVID-19 diagnosis with risk for laboratory-confirmed bloodstream infections (LCBIs, primary outcome), time to LCBI, and risk for death by using logistic and competing risks regression with adjustment for relevant covariates. A total of 10,848 patients were included in the analysis: 918 (8.5%) were given a diagnosis of COVID-19, and 232 (2.1%) had LCBIs during their hospitalization. Of these patients, 58 (25%) were classified as having central line–associated bloodstream infections. After adjusting for covariates, COVID-19–positive status was associated with higher risk for LCBI and death. Reinforcement of infection control practices should be implemented in COVID-19 wards, and review of superiority and inferiority ranking methods by National Healthcare Safety Network criteria might be needed."

Clin Infect Dis: Risk of Healthcare-Associated Transmission of SARS-CoV-2 in Hospitalized Cancer Patients (30 July 2021)

> "Background: There is limited information on the risk of hospital-acquired COVID-19 among high-risk hospitalized patients after exposure to an infected patient or healthcare worker (HCW) in a non-outbreak setting.
>
> Methods: This study was conducted at a tertiary care cancer center in New York City from March 10, 2020, until February 28, 2021. In early April 2020, the study institution implemented universal SARS-CoV-2 testing at admission and retesting every three days through the hospital stay. Contact tracing records were reviewed for all exposures to SARS-CoV-2 positive patients and HCWs.
>
> Results: From March 10, 2020, to February 28, 2021, 11,348 unique patients who were SARS-CoV-2 PCR negative at the time of admission underwent 31,662 post-admission tests during their hospitalization, and 112 tested positive (0.98%). Among these, 49 patients housed in semi-private rooms during admission resulted in 74 close contacts and 14 secondary infections within 14 days, for an overall attack rate of 18.9%. Among those exposed to a roommate undergoing an aerosol-generating procedure (AGP), the attack rate was 35.7%. WGS corroborated transmission in 6/8 evaluated pairs. In addition, three transmission events occurred in 214 patients with significant exposure to 105 COVID-19 positive healthcare workers (1.4%).
>
> Conclusion: The overall risk of hospital-acquired COVID-19 is low for hospitalized cancer patients, even during periods of high community prevalence. However, shared occupancy with an unrecognized case is associated with a high secondary attack rate in exposed roommates."

## Long COVID / Post-COVID Period

### *News in Brief*

"'This Is Really Scary': Kids Struggle With Long Covid: Lingering physical, mental and neurological symptoms are affecting children as well as adults, including many who had mild reactions to the initial coronavirus infection" (NYT [may require login to read]).

Long read: "Perspective – the road to addressing Long Covid" (Science).

## Women's Health, Pregnancy, and Perinatal Care

### *News in Brief*

Citing new safety data, the CDC now recommends COVID-19 vaccination for pregnant people, those who are breastfeeding, or persons trying to get pregnant (CDC).

ACOG and SMFM have also recommended that all pregnant individuals be vaccinated against COVID-19 (ACOG).

### *Journal Articles*

JAMA Netw Open: Characteristics and Outcomes of Women With COVID-19 Giving Birth at US Academic Centers During the COVID-19 Pandemic (11 August 2021)

> "Question  What are the characteristics and outcomes associated with giving birth with COVID-19 over the first year of the pandemic in the US?
>
> Findings  This cohort study examines 869 079 adult women, including 18 715 women with COVID-19, who underwent childbirth at 499 US medical centers between March 1, 2020, and February 28, 2021. Women with COVID-19 had increased mortality, need for intubation and ventilation, and intensive care unit admission.
>
> Meaning  These findings suggest that COVID-19 was associated with increased risk of morbidity and mortality for women giving birth."

JAMA Netw Open: Quantification of Specific Antibodies Against SARS-CoV-2 in Breast Milk of Lactating Women Vaccinated With an mRNA Vaccine (11 August 2021)

> "This cohort study assesses the concentration of SARS-CoV-2 antibodies in the breast milk of women who received vaccines for COVID-19 and their correlation with serum antibody levels...
>
> This study included 33 participants; mean (SD) age and postpartum time were 37.4 (3.3) years and 17.5 (10.1) months, respectively. No participants had confirmed SARS-CoV-2 infection prior to vaccination, nor during the study period (ie, tests for IgG-NC and Ag-RDT were all negative). We collected and analyzed 93 serum and milk samples from the 33 participants….
>
> Our results suggest that breast milk from women vaccinated with the novel mRNA-based Pfizer-BioNTech vaccine contains specific anti–SARS-CoV-2 IgG(S1) antibodies. Furthermore, we found that after the second dose, breast milk IgG(S1) levels increased and were positively associated with corresponding serum levels."

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JAMA Netw Open: SARS-CoV-2 Infection Among Maternal-Infant Dyads in Ontario, Canada (09 August 2021)

> "This cohort study uses population-based health data to assess SARS-CoV-2 testing outcomes among infants born in Ontario, Canada, during 9 months of the 2020 COVID-19 pandemic to mothers with confirmed infection at delivery....
>
> Only 156 of 82 484 delivering mothers (0.2%) were known to be positive for SARS-CoV-2 infection within 2 weeks of delivery. Only 6 infants (3.9%) born to these positive mothers were known to have acquired SARS-CoV-2 perinatally, and another 9 (5.8%) had positive tested results later in early infancy."

Emerg Infect Dis: Severe Acute Respiratory Syndrome Coronavirus 2 and Pregnancy Outcomes According to Gestational Age at Time of Infection (05 August 2021)

> "We conducted an international multicenter retrospective cohort study, PregOuTCOV, to examine the effect of gestational age at time of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on obstetric and neonatal outcomes. We included all singleton pregnancies with a live fetus at 10 weeks' gestation in which pregnancy outcomes were known. The exposed group consisted of patients infected with SARS-CoV-2, whereas the unexposed group consisted of all remaining patients during the same period. Primary outcomes were defined as composite adverse obstetric outcomes and composite adverse neonatal outcomes. Of 10,925 pregnant women, 393 (3.60%) were infected with SARS-CoV-2 (exposed group). After matching for possible confounders, we identified statistically significant increases in the exposed group of composite adverse obstetric outcomes at >20 weeks' gestation and of composite adverse neonatal outcomes at >26 weeks' gestation ($p<0.001$). Vaccination programs should target women early in pregnancy or before conception, if possible."

CMAJ: Preterm birth and stillbirth rates during the COVID-19 pandemic: a population-based cohort study (03 August 2021)

> "BACKGROUND: Conflicting reports have emerged for rates of preterm births and stillbirths during the COVID-19 pandemic. Most of these reports did not account for natural variation in these rates. We aimed to evaluate variations in preterm birth and stillbirth rates before and during the COVID-19 pandemic in Ontario, Canada.
>
> METHODS: We conducted a retrospective cohort study using linked population health administrative databases of pregnant people giving birth in any hospital in Ontario between July 2002 and December 2020. We calculated preterm birth and stillbirth rates. We assessed preterm birth at 22–28, 29–32 and 33–36 weeks' gestation, and stillbirths at term and preterm gestation. We used Laney control P' charts for the 18-year study period (6-mo

> observation periods) and interrupted time-series analyses for monthly rates for the most recent 4 years.
>
> RESULTS: We evaluated 2 465 387 pregnancies, including 13 781 that resulted in stillbirth. The mean preterm birth rate for our cohort was 7.96% (range 7.32%–8.59%). From January to December 2020, we determined that the preterm birth rate in Ontario was 7.87%, with no special cause variation. The mean stillbirth rate for the cohort was 0.56% (range 0.48%–0.70%). From January to December 2020, the stillbirth rate was 0.53%, with no special cause variation. We did not find any special cause variation for preterm birth or stillbirth subgroups. We found no changes in slope or gap between prepandemic and pandemic periods using interrupted time-series analyses.
>
> INTERPRETATION: In Ontario, Canada, we found no special cause variation (unusual change) in preterm birth or stillbirth rates, overall or by subgroups, during the first 12 months of the COVID-19 pandemic compared with the previous 17.5 years."

## Pediatric Population

### *News in Brief*

The AAP has released updated guidance on preventing RSV during the delayed season, assumed to because of COVID-19 mitigation measures (AAP).

"Delta is bad news for kids: More children are falling ill because more are being infected" (Atlantic).

### *Special Reports and Other Resources*

ASPR TRACIE: Pediatric Lessons Learned from COVID-19: Immediate and Future Implications [pdf] (July 2021)

> This document includes links to a speaker series with slides, recorded webinars, and other resources.
>
> The special focus is "Suicide and Mental Health Emergencies Before, During, and Beyond COVID-19". It also has other recordings on disaster pediatric triage, tools for coping with school, and pandemic impact on children.

## *Journal Articles*

NEJM: Evaluation of mRNA-1273 SARS-CoV-2 Vaccine in Adolescents (11 August 2021)

> "Background: The incidence of coronavirus disease 2019 (Covid-19) among adolescents between 12 and 17 years of age was approximately 900 per 100,000 population from April 1 through June 11, 2021. The safety, immunogenicity, and efficacy of the mRNA-1273 vaccine [Moderna] in adolescents are unknown.
>
> Methods: In this ongoing phase 2-3, placebo-controlled trial, we randomly assigned healthy adolescents (12 to 17 years of age) in a 2:1 ratio to receive two injections of the mRNA-1273 vaccine (100 µg in each) or placebo, administered 28 days apart. The primary objectives were evaluation of the safety of mRNA-1273 in adolescents and the noninferiority of the immune response in adolescents as compared with that in young adults (18 to 25 years of age) in a phase 3 trial. Secondary objectives included the efficacy of mRNA-1273 in preventing Covid-19 or asymptomatic severe acute respiratory syndrome coronavirus 2 infection.
>
> Results: A total of 3732 participants were randomly assigned to receive mRNA-1273 (2489 participants) or placebo (1243 participants). In the mRNA-1273 group, the most common solicited adverse reactions after the first or second injections were injection-site pain (in 93.1% and 92.4%, respectively), headache (in 44.6% and 70.2%, respectively), and fatigue (in 47.9% and 67.8%, respectively); in the placebo group, the most common solicited adverse reactions after the first or second injections were injection-site pain (in 34.8% or 30.3%, respectively), headache (in 38.5% and 30.2%, respectively), and fatigue (in 36.6% and 28.9%, respectively). No serious adverse events related to mRNA-1273 or placebo were noted. The geometric mean titer ratio of pseudovirus neutralizing antibody titers in adolescents relative to young adults was 1.08 (95% confidence interval [CI], 0.94 to 1.24), and the absolute difference in serologic response was 0.2 percentage points (95% CI, -1.8 to 2.4), which met the noninferiority criterion. No cases of Covid-19 with an onset of 14 days after the second injection were reported in the mRNA-1273 group, and four cases occurred in the placebo group.
>
> Conclusions: The mRNA-1273 vaccine had an acceptable safety profile in adolescents. The immune response was similar to that in young adults, and the vaccine was efficacious in preventing Covid-19."

JAMA Pediatr: Global Prevalence of Depressive and Anxiety Symptoms in Children and Adolescents During COVID-19: A Meta-analysis (09 August 2021)

> "Question What is the global prevalence of clinically elevated child and adolescent anxiety and depression symptoms during COVID-19?

> Findings In this meta-analysis of 29 studies including 80 879 youth globally, the pooled prevalence estimates of clinically elevated child and adolescent depression and anxiety were 25.2% and 20.5%, respectively. The prevalence of depression and anxiety symptoms during COVID-19 have doubled, compared with prepandemic estimates, and moderator analyses revealed that prevalence rates were higher when collected later in the pandemic, in older adolescents, and in girls.
>
> Meaning The global estimates of child and adolescent mental illness observed in the first year of the COVID-19 pandemic in this study indicate that the prevalence has significantly increased, remains high, and therefore warrants attention for mental health recovery planning."

Lancet Child Adolesc Health: Illness duration and symptom profile in symptomatic UK school-aged children tested for SARS-CoV-2 (03 August 2021)

> "Background: In children, SARS-CoV-2 infection is usually asymptomatic or causes a mild illness of short duration. Persistent illness has been reported; however, its prevalence and characteristics are unclear. We aimed to determine illness duration and characteristics in symptomatic UK school-aged children tested for SARS-CoV-2 using data from the COVID Symptom Study, one of the largest UK citizen participatory epidemiological studies to date.
>
> Methods: In this prospective cohort study, data from UK school-aged children (age 5-17 years) were reported by an adult proxy. Participants were voluntary, and used a mobile application (app) launched jointly by Zoe Limited and King's College London. Illness duration and symptom prevalence, duration, and burden were analysed for children testing positive for SARS-CoV-2 for whom illness duration could be determined, and were assessed overall and for younger (age 5-11 years) and older (age 12-17 years) groups. Children with longer than 1 week between symptomatic reports on the app were excluded from analysis. Data from symptomatic children testing negative for SARS-CoV-2, matched 1:1 for age, gender, and week of testing, were also assessed.
>
> Findings: 258 790 children aged 5-17 years were reported by an adult proxy between March 24, 2020, and Feb 22, 2021, of whom 75 529 had valid test results for SARS-CoV-2. 1734 children (588 younger and 1146 older children) had a positive SARS-CoV-2 test result and calculable illness duration within the study timeframe (illness onset between Sept 1, 2021, and Jan 24, 2021). The most common symptoms were headache (1079 [62·2%] of 1734 children), and fatigue (954 [55·0%] of 1734 children). Median illness duration was 6 days (IQR 3-11) versus 3 days (2-7) in children testing negative, and was positively associated with age (Spearman's rank-order rs 0·19, p<0·0001). Median illness duration was longer for older children (7 days, IQR 3-12) than younger children (5 days, 2-9). 77 (4·4%) of 1734 children had illness duration of at least 28 days, more commonly in older than younger children (59 [5·1%] of 1146 older children vs 18 [3·1%] of 588 younger children; p=0·046).

> The commonest symptoms experienced by these children during the first 4 weeks of illness were fatigue (65 [84·4%] of 77), headache (60 [77·9%] of 77), and anosmia (60 [77·9%] of 77); however, after day 28 the symptom burden was low (median 2 symptoms, IQR 1-4) compared with the first week of illness (median 6 symptoms, 4-8). Only 25 (1·8%) of 1379 children experienced symptoms for at least 56 days. Few children (15 children, 0·9%) in the negatively tested cohort had symptoms for at least 28 days; however, these children experienced greater symptom burden throughout their illness (9 symptoms, IQR 7·7-11·0 vs 8, 6-9) and after day 28 (5 symptoms, IQR 1·5-6·5 vs 2, 1-4) than did children who tested positive for SARS-CoV-2.
>
> Interpretation: Although COVID-19 in children is usually of short duration with low symptom burden, some children with COVID-19 experience prolonged illness duration. Reassuringly, symptom burden in these children did not increase with time, and most recovered by day 56. Some children who tested negative for SARS-CoV-2 also had persistent and burdensome illness. A holistic approach for all children with persistent illness during the pandemic is appropriate."

Virol J: Impact of COVID-19 pandemic on the prevalence of respiratory viruses in children with lower respiratory tract infections in China (03 August 2021)

> "Background: The multifaceted non-pharmaceutical interventions (NPIs) taken during the COVID-19 pandemic not only decrease the spreading of the SARS-CoV-2, but have impact on the prevalence of other viruses. This study aimed to explore the prevalence of common respiratory viruses among hospitalized children with lower respiratory tract infections (LRTI) in China during the COVID-19 pandemic.
>
> Methods: Respiratory specimens were obtained from children with LRTI at Children's Hospital of Fudan University for detection of respiratory syncytial virus (RSV), adenovirus (ADV), parainfluenza virus (PIV) 1 to 3, influenza virus A (FluA), influenza virus B (FluB), human metapneumovirus (MPV) and rhinovirus (RV). The data were analyzed and compared between the year of 2020 (COVID-19 pandemic) and 2019 (before COVID-19 pandemic).
>
> Results: A total of 7107 patients were enrolled, including 4600 patients in 2019 and 2507 patients in 2020. Compared with 2019, we observed an unprecedented reduction of RSV, ADV, FluA, FluB, and MPV infections in 2020, despite of reopening of schools in June, 2020. However, the RV infection was significantly increased in 2020 and a sharp increase was observed especially after reopening of schools. Besides, the PIV infection showed resurgent characteristic after September of 2020. The mixed infections were significantly less frequent in 2020 compared with the year of 2019.

> Conclusions: The NPIs during the COVID-19 pandemic have great impact on the prevalence of common respiratory viruses in China. Meanwhile, we do need to be cautious of a possible resurgence of some respiratory viruses as the COVID-19 restrictions are relaxed."

Br J Ophthalmol: Myopia incidence and lifestyle changes among school children during the COVID-19 pandemic: a population-based prospective study (02 August 2021)

> "Background: The impacts of social restrictions for COVID-19 on children's vision and lifestyle remain unknown.
>
> Aims: To investigate myopia incidence, spherical equivalent refraction (SER) and lifestyle changes among schoolchildren during the COVID-19 pandemic.
>
> Methods: Two separate longitudinal cohorts of children aged 6-8 years in Hong Kong were included. The COVID-19 cohort was recruited at the beginning of the COVID-19 outbreak, whereas the pre-COVID-19 cohort was recruited before the COVID-19 pandemic. All children received ocular examinations, and answered a standardised questionnaire relating to their lifestyle, including time spent on outdoor activities and near work, both at baseline and at follow-up visits.
>
> Results: A total of 1793 subjects were recruited, of whom 709 children comprised the COVID-19 cohort with 7.89±2.30 months of follow-up, and 1084 children comprised the pre-COVID-19 cohort with 37.54±3.12 months of follow-up. The overall incidence was 19.44% in the COVID-19 cohort, and 36.57% in pre-COVID-19 cohort. During the COVID-19 pandemic, the change in SER and axial length was -0.50±0.51 D and 0.29±0.35 mm, respectively; the time spent on outdoor activities decreased from 1.27±1.12 to 0.41±0.90 hours/day ($p<0.001$), while screen time increased from 2.45±2.32 to 6.89±4.42 hours/day ($p<0.001$).
>
> Conclusions: We showed a potential increase in myopia incidence, significant decrease in outdoor time and increase in screen time among schoolchildren in Hong Kong during the COVID-19 pandemic. Our results serve to warn eye care professionals, and also policy makers, educators and parents, that collective efforts are needed to prevent childhood myopia-a potential public health crisis as a result of COVID-19."

JAMA Pediatr: Setting Priorities to Address Research Gaps in Long-term COVID-19 Outcomes in Children (02 August 2021)

> "This Viewpoint describes gaps in research on long-term COVID-19 outcomes in children and provides recommendations to address these gaps….
>
> Our goal is to make recommendations to address the gaps in research on long-term COVID-19 outcomes in children. The research priorities on physical, cognitive, psychological, and social impact of COVID-19 in children need to be identified within a systems framework and coordinated at a national and international level."

## Healthcare Workers

### *News in Brief*

"Vaccine refusers risk compassion fatigue: After the horrors that health-care workers have endured during the pandemic, many are struggling to sympathize with people who won't protect themselves" (Atlantic).

### *Journal Articles*

Infect Control Hosp Epidemiol: Transmission of SARS CoV2 among health careworkers (HCW) during three waves of the SARS-CoV 2 pandemic in Germany: Results of an anonymous survey (02 August 2021)

> "In order to learn more about the transmission of SARS CoV2 among HCP we conducted and anonymous survey which was distributed by mass e-mail though interested infection control practitioners (IP) to all employees in their respective institution….
>
> In summary unprotected contacts off work and with undiagnosed patients or fellow health care workers during work seem to be a major driver of SARS-CoV2-infections among HCW, making general protective measures a necessity at least until fully vaccination status is reached."

Infect Control Hosp Epidemiol: Incidence rate of SARS-CoV-2 among nurses in COVID-19 units vs. non-COVID-19-units at a large academic medical center (02 August 2021)

> "Here, we aimed to longitudinally characterize the incidence of SARS-CoV-2 infections among nurses working in COVID-19 units vs. non-COVID-19 units throughout the first year of the pandemic….
>
> In this observational study, the incidence of SARS-CoV-2 positivity among nurses assigned to COVID-19 units was remarkably similar to non-COVID-19 units, except during April 2020. Interestingly, universal goggles and masking were made mandatory on April 23, 2020, and thus we strongly believe this was the factor that decreased the infection rates in COVID-19 units. Notably, during the fall months with highest incidence of COVID-19 in the community, the incidence rate of SARS-CoV-2 among nurses was the same regardless of their unit, suggesting community exposures rather than hospital-based exposures."

Infect Control Hosp Epidemiol: COVID-19 risk among healthcare workers performing nasopharyngeal testing (02 August 2021)

> "We performed a multicenter cross-sectional study across four CACs in Toronto, Canada. Each CAC prospectively identified HCWs with COVID-19 between 15 March, 2020 and 14 March, 2021. All asymptomatic HCWs working in the CACs [COVID-19 Assessment Centres]

> were required to undergo SARS-CoV-2 testing if they had an unprotected close contact with anyone with COVID-19, travel, or if they developed any symptoms whether minimal or atypical…
>
> Our results show that when embedded within a comprehensive bundle of measures designed to minimize COVID-19 transmission, the use of surgical masks was effective in protecting HCWs given a rate of infection similar to a population average that included non-essential workers. The similar infection rates between clinical and non-clinical staff suggests that most infections that did occur were likely acquired outside of the CACs."

## Mental Health, Psychosocial Issues, and Wellness

### *Journal Articles*

Prehosp Disaster Med: Effects of the COVID-19 Pandemic on the Intimate Partner Violence and Sexual Function: A Systematic Review (27 July 2021)

> "Introduction: The pandemic caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), or coronavirus disease 2019 (COVID-19), has affected many people in the world and has impacted the physical, social, and mental health of the world population. One of these psychological consequences is intimate partner violence affecting sexual health.
>
> Methods: This study was performed as a systematic review on the effect of the SARS-CoV-2 pandemic on sexual function and domestic violence in the world. Accordingly, all English-language studies conducted from the beginning of the SARS-CoV-2 pandemic to the end of 2020 were extracted by searching in the Scopus, Web of Science, PubMed (including Medline), Cochrane Library, and Science Direct databases and then reviewed. The quality of the articles was assessed using the STROBE checklist.
>
> Results: A total of 11 studies were included in the systematic review. Accordingly, domestic violence during the exposure to COVID-19 had increased. Moreover, the mean scores of sexual function and its components had reduced at the time of exposure to the pandemic compared to before.
>
> Conclusion: Given the potential long-term effects of the coronavirus crisis and the large population being affected by this disease, strategies to promote sexual health and fertility of families to prevent or further reduce violence and sexual functions should be chosen."

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Psychol Med: Acute and longer-term psychological distress associated with testing positive for COVID-19: longitudinal evidence from a population-based study of US adults (26 July 2021)

> "Background: The novel coronavirus (SARS-CoV-2) has produced a considerable public health burden but the impact that contracting the disease has on mental health is unclear. In this observational population-based cohort study, we examined longitudinal changes in psychological distress associated with testing positive for coronavirus disease 2019 (COVID-19).
>
> Methods: Participants (N = 8002; observations = 139 035) were drawn from 23 waves of the Understanding America Study, a nationally representative probability-based online panel of American adults followed-up every 2 weeks from 1 April 2020 to 15 February 2021. Psychological distress was assessed using the standardized total score on the Patient Health Questionnaire-4.
>
> Results: Over the course of the study, 576 participants reported testing positive for COVID-19. Using regression analysis including individual and time-fixed effects we found that psychological distress increased by 0.29 standard deviations ($p < 0.001$) during the 2-week period when participants first tested positive for COVID-19. Distress levels remained significantly elevated ($d = 0.16$, $p < 0.01$) for a further 2 weeks, before returning to baseline levels. Coronavirus symptom severity explained changes in distress attributable to COVID-19, whereby distress was more pronounced among those whose symptoms were more severe and were slower to subside.
>
> Conclusions: This study indicates that testing positive for COVID-19 is associated with an initial increase in psychological distress that diminishes quickly as symptoms subside. Although COVID-19 may not produce lasting psychological distress among the majority of the general population it remains possible that a minority may suffer longer-term mental health consequences."

## Disparities and Health Equity

### *Journal Articles*

MMWR: Alternative Methods for Grouping Race and Ethnicity to Monitor COVID-19 Outcomes and Vaccination Coverage (13 August 2021)

> "What is already known about this topic? Analyses of race and ethnicity in COVID-19 data to identify and monitor disparities are complicated by missing or unknown data.

> What is added by this report? Methods that use more race information when ethnicity information is missing resulted in higher estimated COVID-19 case counts, incidence, and vaccination coverage for most racial groups studied; however, these methods have limitations and warrant further examination of potential bias.
>
> What are the implications for public health practice? Ongoing work with experts is needed to identify methods for optimizing race and ethnicity data when data are incomplete. Multiple data sources are needed to monitor disparities and continued efforts are needed to strengthen the reporting of these data, consistent with CDC's Data Modernization Initiative."

PNAS: Socioeconomic privilege and political ideology are associated with racial disparity in COVID-19 vaccination (29 July 2021)

> "Vaccine uptake is critical for mitigating the impact of COVID-19 in the United States, but structural inequities pose a serious threat to progress. Racial disparities in vaccination persist despite the increased availability of vaccines. We ask what factors are associated with such disparities. We combine data from state, federal, and other sources to estimate the relationship between social determinants of health and racial disparities in COVID-19 vaccinations at the county level.
>
> Analyzing vaccination data from 19 April 2021, when nearly half of the US adult population was at least partially vaccinated, we find associations between racial disparities in COVID-19 vaccination and median income (negative), disparity in high school education (positive), and vote share for the Republican party in the 2020 presidential election (negative), while vaccine hesitancy is not related to disparities. We examine differences in associations for COVID-19 vaccine uptake as compared with influenza vaccine. Key differences include an amplified role for socioeconomic privilege factors and political ideology, reflective of the unique societal context in which the pandemic has unfolded."

## Risk, Transmission, and Exposure

### *News in Brief*

"Masks are back, maybe for the long term: Some people can't help but feel that masking while vaccinated is a regression—especially because this time, there's no obvious off-ramp" (Atlantic).

## *Journal Articles*

### *Aerosols*

Clin Infect Dis: Viral Load of SARS-CoV-2 in Respiratory Aerosols Emitted by COVID-19 Patients while Breathing, Talking, and Singing (06 August 2021)

> "Background: Multiple SARS-CoV-2 superspreading events suggest that aerosols play an important role in driving the COVID-19 pandemic. To better understand how airborne SARS-CoV-2 transmission occurs, we sought to determine viral loads within coarse (>5µm) and fine (≤5µm) respiratory aerosols produced when breathing, talking, and singing.
>
> Methods: Using a G-II exhaled breath collector, we measured viral RNA in coarse and fine respiratory aerosols emitted by COVID-19 patients during 30 minutes of breathing, 15 minutes of talking, and 15 minutes of singing.
>
> Results: Thirteen participants (59%) emitted detectable levels of SARS-CoV-2 RNA in respiratory aerosols, including 3 asymptomatic and 1 presymptomatic patient. Viral loads ranged from 63-5,821 N gene copies per expiratory activity per participant, with high person-to-person variation. Patients earlier in illness were more likely to emit detectable RNA. Two participants, sampled on day 3 of illness, accounted for 52% of the total viral load. Overall, 94% of SARS-CoV-2 RNA copies were emitted by talking and singing. Interestingly, 7 participants emitted more virus from talking than singing. Overall, fine aerosols constituted 85% of the viral load detected in our study. Virus cultures were negative.
>
> Conclusions: Fine aerosols produced by talking and singing contain more SARS-CoV-2 copies than coarse aerosols and may play a significant role in SARS-CoV-2 transmission. Exposure to fine aerosols, especially indoors, should be mitigated. Isolating viable SARS-CoV-2 from respiratory aerosol samples remains challenging, and whether this can be more easily accomplished for emerging SARS-CoV-2 variants is an urgent enquiry necessitating larger-scale studies."

Environ Sci Pollut Res Int: The detection of SARS-CoV-2 RNA in indoor air of dental clinics during the COVID-19 pandemic (03 August 2021)

> "In the indoor environment of dental clinics, dental personnel and patients are exposed to a risk of infection because of the transmission of SARS-CoV-2 via particles or droplets. This study investigated the presence of SARS-CoV-2 RNA in indoor air of dental clinics in Tehran, Iran. Air sampling was done (n = 36) collecting particulate samples on PTFE filters at flow rates of 30 to 58 L/min. The samples were analyzed with novel coronavirus nucleic acid diagnostic real-time PCR kits. Only 13 out of 36 samples were positive for SARS-CoV-2 RNA. Logistic regression showed that sampling site's volume, PM2.5 concentration, number of people, and number of active patient treatment units were significantly positively related with the presence of SARS-CoV-2 RNA. Thus, strategies to control the spread of COVID-19

> should include reducing the number of infected people in dental clinics, adding filtration systems, and/or improving ventilation conditions."

*Prophylaxis*

NEJM: Subcutaneous REGEN-COV Antibody Combination to Prevent Covid-19 (04 August 2021)

> "Background: REGEN-COV (previously known as REGN-COV2), a combination of the monoclonal antibodies casirivimab and imdevimab, has been shown to markedly reduce the risk of hospitalization or death among high-risk persons with coronavirus disease 2019 (Covid-19). Whether subcutaneous REGEN-COV prevents severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and subsequent Covid-19 in persons at high risk for infection because of household exposure to a person with SARS-CoV-2 infection is unknown.
>
> Methods: We randomly assigned, in a 1:1 ratio, participants (≥12 years of age) who were enrolled within 96 hours after a household contact received a diagnosis of SARS-CoV-2 infection to receive a total dose of 1200 mg of REGEN-COV or matching placebo administered by means of subcutaneous injection. At the time of randomization, participants were stratified according to the results of the local diagnostic assay for SARS-CoV-2 and according to age. The primary efficacy end point was the development of symptomatic SARS-CoV-2 infection through day 28 in participants who did not have SARS-COV-2 infection (as measured by reverse-transcriptase-quantitative polymerase-chain-reaction assay) or previous immunity (seronegativity).
>
> Results: Symptomatic SARS-CoV-2 infection developed in 11 of 753 participants in the REGEN-COV group (1.5%) and in 59 of 752 participants in the placebo group (7.8%) (relative risk reduction [1 minus the relative risk], 81.4%; P<0.001). In weeks 2 to 4, a total of 2 of 753 participants in the REGEN-COV group (0.3%) and 27 of 752 participants in the placebo group (3.6%) had symptomatic SARS-CoV-2 infection (relative risk reduction, 92.6%). REGEN-COV also prevented symptomatic and asymptomatic infections overall (relative risk reduction, 66.4%). Among symptomatic infected participants, the median time to resolution of symptoms was 2 weeks shorter with REGEN-COV than with placebo (1.2 weeks and 3.2 weeks, respectively), and the duration of a high viral load (>104 copies per milliliter) was shorter (0.4 weeks and 1.3 weeks, respectively). No dose-limiting toxic effects of REGEN-COV were noted.
>
> Conclusions: Subcutaneous REGEN-COV prevented symptomatic Covid-19 and asymptomatic SARS-CoV-2 infection in previously uninfected household contacts of infected persons. Among the participants who became infected, REGEN-COV reduced the duration of symptomatic disease and the duration of a high viral load."

*Transmission*

Sci Rep: Rates of SARS-CoV-2 transmission and vaccination impact the fate of vaccine-resistant strains (30 July 2021)

> "Vaccines are thought to be the best available solution for controlling the ongoing SARS-CoV-2 pandemic. However, the emergence of vaccine-resistant strains may come too rapidly for current vaccine developments to alleviate the health, economic and social consequences of the pandemic. To quantify and characterize the risk of such a scenario, we created a SIR-derived model with initial stochastic dynamics of the vaccine-resistant strain to study the probability of its emergence and establishment. Using parameters realistically resembling SARS-CoV-2 transmission, we model a wave-like pattern of the pandemic and consider the impact of the rate of vaccination and the strength of non-pharmaceutical intervention measures on the probability of emergence of a resistant strain. As expected, we found that a fast rate of vaccination decreases the probability of emergence of a resistant strain. Counterintuitively, when a relaxation of non-pharmaceutical interventions happened at a time when most individuals of the population have already been vaccinated the probability of emergence of a resistant strain was greatly increased. Consequently, we show that a period of transmission reduction close to the end of the vaccination campaign can substantially reduce the probability of resistant strain establishment. Our results suggest that policymakers and individuals should consider maintaining non-pharmaceutical interventions and transmission-reducing behaviours throughout the entire vaccination period."

Environ Res: Transmission risks of respiratory infectious diseases in various confined spaces: A meta-analysis for future pandemics (12 July 2021)

> "Background: If the different transmission risks of respiratory infectious diseases according to the type of confined space and associated factors could be discovered, this kind of information will be an important basis for devising future quarantine policies. However, no comprehensive systematic review or meta-analysis for this topic exists.
>
> Objective: The objective of this study is to analyze different transmission risks of respiratory infectious diseases according to the type of confined space. This information will be an important basis for devising future quarantine policies.
>
> Methods: A medical librarian searched MEDLINE, EMBASE, and the Cochrane Library (until December 01, 2020).
>
> Results: A total of 147 articles were included. The risk of transmission in all types of confined spaces was approximately 3 times higher than in open space (combined RR, 2.95 (95% CI 2.62-3.33)). Among them, school or workplace showed the highest transmission risk (combined RR, 3.94 (95% CI 3.16-4.90)). Notably, in the sub-analysis for SARS-CoV-2,

> residential space and airplane were the riskiest space (combined RR, 8.30 (95% CI 3.30-20.90) and 7.30 (95% CI 1.15-46.20), respectively).
>
> Discussion: Based on the equation of the total number of contacts, the order of transmission according to the type of confined space was calculated. The calculated order was similar to the observed order in this study. The transmission risks in confined spaces can be lowered by reducing each component of the aforementioned equation. However, as seen in the data for SARS-CoV-2, the closure of one type of confined space could increase the population density in another confined space. The authority of infection control should consider this paradox. Appropriate quarantine measures targeted for specific types of confined spaces with a higher risk of transmission, school or workplace for general pathogens, and residential space/airplane for SARS-CoV-2 can reduce the transmission of respiratory infectious diseases."

*Travel Risk*

Clin Infect Dis: Epidemiology and risk of COVID-19 among travelers at airport and port quarantine stations across Japan: a nationwide descriptive analysis and an individually matched case-control study (28 July 2021)

> "Background: The epidemiology and risk of COVID-19 among travelers at international borders remain unclear.
>
> Methods: We conducted descriptive and individually matched case-control studies using a nationwide register for COVID-19 testing of travelers from August 3 to October 31, 2020 at airport/port quarantine stations across Japan. Cases defined as COVID-19-positive travelers on arrival were individually matched with four controls for arrival date and airport/port. We assessed associations between test positivity and traveler characteristics using conditional logistic regression.
>
> Results: Overall, 157,507 travelers arriving from 146 countries/areas at 17 quarantine stations across Japan were tested for COVID-19. The test percent positivity during the study period was 0.35%. In the case-control study with 536 cases and 2,144 controls, we found evidence of lower test positivity in travelers aged 3-19 years, females, and travel corridor users (adjusted odds ratio [95% confidence interval]: 0.36 [0.22-0.60], 0.71 [0.56-0.89], and 0.48 [0.30-0.77], respectively), whereas higher positivity was associated with arrival from South-East Asia (1.88 [1.33-2.65]) or lower-middle- or low-income countries (2.46 [1.69-3.58] and 7.25 [2.22-23.66], respectively), any symptom (4.08 [1.43-11.65]), and nasopharyngeal compared to saliva sampling (2.75 [1.85-4.09]). A higher 14-day average incidence in the countries of stay was also associated with higher test positivity (1.64 [1.16-2.33] and 3.13 [1.88-5.23]).

> Conclusions: These findings justify travel restrictions based on the epidemic situation in countries of stay, although underestimation of the epidemic in lower income countries should be considered. A strict travel corridor could also reduce COVID-19 importation risk."

## Other Infectious Diseases

### *News in Brief*

The CDC "has confirmed a new fatal case of the rare disease melioidosis in Georgia that is linked to three previous cases in different states" (CDC statement; see also: CDC HAN).

The CDC and FDA are looking into a multistate outbreak of *Burkholderia cepacia* from contaminated ultrasound gel (CDC).

"The Beijing Center for Disease Control and Prevention (Beijing CDC) reported Monday a human inhalation anthrax case in a patient" (ONT).

"West Africa's first-ever case of Marburg virus disease confirmed in Guinea" (WHO).

"Nigeria reports 4 additional confirmed monkeypox cases in July" (ONT). Luckily, no new cases have been detected in the US after the CDC monitored contacts of the case here (STAT).

"Parts of Lake Tahoe closed after chipmunks test positive for plague" (NBC).

Some good news amid all this… "'Landmark' study finds artificial antibodies can protect against malaria" (Science).

### *Journal Articles*

J R Soc Med: Veterinary intelligence: integrating zoonotic threats into global health security (05 August 2021)

> "Zoonotic diseases are leading threats to public health globally. The recent G7 meeting of world leaders made strong political commitments to strengthening One Health approaches at the human–animal interface as an integral element of the global health security architecture. Repeated epidemics and pandemics from Ebola to COVID-19 have demonstrated the systematic disregard of zoonotic disease within what still remains a predominantly human-centric public health approach. In particular, commitments to the expansion of pathogen surveillance and health intelligence require the development of novel approaches to improve and strengthen our domestic capabilities for species neutral monitoring, which requires the sustained involvement of veterinary colleagues."

## Special Topic: Climate Change

*Earlier this month, the United Nations released a major report on climate change (see link in Special Reports, below). Because of the news coverage and intersections with the pandemic and military concerns, I have included this special topic section to highlight some of the issues and literature on climate change.*

*If you are interested in this literature, the NIH's National Institute of Environmental Health Sciences has the* Climate Change and Human Health Literature Portal*, which is "[an] integrated, curated bibliographic database of global peer-reviewed research and gray literature on the science of climate impacts on human health".*

*-- Tracy Shields, Reference Medical Librarian*

### ***News in Brief***

*The Report*

"IPCC climate report: Earth is warmer than it's been in 125,000 years: Landmark assessment says that greenhouse gases are unequivocally driving extreme weather — but that nations can still prevent the worst impacts" (Nature).

"3 things to know about what scientists say about our future climate" (NPR).

"It's grim. The latest UN report is clear: Climate change is here, it's a crisis, and it's caused by fossil fuels" (Atlantic).

*Weather*

Case in point: "Nearly 2 in 3 Americans are dealing with dangerous heat waves" (NPR) and "Sicily may have experienced the hottest day ever in Europe" (NPR).

Major weather events or environmental effects associated with climate change could be driving infectious disease outbreaks – like West Nile virus – too: "alarming side effect of US drought: Stagnant water caused by dry weather gives mosquitoes – the insect that spreads the virus – free rein, leading to an increased risk for humans" (Guardian).

*Military*

Long read: "Climate change is already disrupting the military. It will get worse, officials say: Even as wildfires drain National Guard resources, the Pentagon is racing to develop computer models that can better guide decisions about sustainability efforts" (Defense One).

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### *Special Reports and Other Resources*

IPCC: AR6 Climate Change 2021: The Physical Science Basis (07 August 2021)

> This report is the first of three, with the next 2 planned for release early next year.
>
> "The Working Group I contribution to the Sixth Assessment Report addresses the most up-to-date physical understanding of the climate system and climate change, bringing together the latest advances in climate science, and combining multiple lines of evidence from paleoclimate, observations, process understanding, and global and regional climate simulations….
>
> The Summary for Policymakers (SPM) provides a high-level summary of the understanding of the current state of the climate, including how it is changing and the role of human influence, and the state of knowledge about possible climate futures, climate information relevant to regions and sectors, and limiting human-induced climate change."

IMCCS: The World Climate and Security Report 2021 [pdf] (June 2021)

> "The World Climate and Security Report (WCSR) 2021 from the Expert Group of the International Military Council on Climate and Security is a global assessment of the security dimensions of a changing climate and effective means to address them. It is intended to inform timely climate and security policy and action, and builds upon the analysis in the first WCSR, released in February 2020.
>
> The world is at an inflection point for global climate action. Since the inaugural WCSR was released at the Munich Security Conference last year, we have witnessed a shift in awareness and growing acceptance of the security dimension of climate. It is now time to turn that awareness into action, driven by a sense of urgency amongst nations and other essential actors to address climate security risks. The key finding of the report is that a transition to more robust implementation of climate security practices is critical.
>
> To that end, in addition to deep dive risk assessments of Europe and sub-Saharan Africa, the second edition of the WCSR provides concrete tools to help policymakers begin that transition, as they work to assess and address climate security risks and opportunities. Key among them is a first of its kind Climate Security Risk Matrix methodology, which evaluates comparative risk among countries. The report also includes a comprehensive assessment of existing climate security practices, and the findings from the second annual Climate Security Risk Perception Survey of top climate security experts. Both will assist policymakers in evaluating and prioritizing next steps needed to both prepare for and prevent climate security risks. Now more than ever, climate change is a critical aspect of national and global security, requiring collective global action to meet this unprecedented threat."

### *Journal Articles*

#### *Editorials*

Acad Med: Preparing the Next Generation of Health Professionals to Tackle Climate Change (10 August 2021)

J Pediatr: Climate change and environmental pollution induced risks on children's health: are pediatricians prepared to meet the challenge? (09 August 2021)

#### *Mental Health*

Psychiatr Serv: Climate Change and Mental Health: Implications for the Psychiatric Workforce (09 August 2021)

> "Climate change is a major global public mental health crisis that is expected to increase the need for mental health services. Psychiatrists and other mental health care providers must address workforce needs through recruitment, training and education, prevention and intervention, public policy and advocacy, and direct efforts to reduce climate change. This column discusses concrete steps for the psychiatric workforce to take to prepare for growing mental health needs associated with climate change."

#### *Health Outcomes*

J Occup Environ Med: Improving Patient Outcomes in the Dual Crises of Climate Change and COVID-19: Proceedings of the Third Annual Clinical Climate Change Meeting, January 8, 2021 (04 August 2021)

> "The tremendous global toll of the COVID-19 pandemic does not fall equally on all populations. Indeed, this crisis has exerted more severe impacts on the most vulnerable communities, spotlighting the continued consequences of longstanding structural, social, and healthcare inequities. This disparity in COVID-19 parallels the unequal health consequences of climate change, whereby underlying inequities perpetuate adverse health outcomes disproportionately among vulnerable populations. As these two crises continue to unfold, there is an urgent need for healthcare practitioners to identify and implement solutions to mitigate adverse health outcomes, especially in the face of global crises. To support this need, the 2021 Clinical Climate Change Conference held a virtual meeting to discuss the implications of the convergence of the climate crisis and COVID-19, particularly for vulnerable patient populations and the clinicians who care for them. Presenters and panelists provided evidence-based solutions to help health professionals improve and adapt their practice to these evolving scenarios. Together, participants explored community

health system and national solutions to reduce the impacts of COVID-19 and the climate crisis, to promote community advocacy, and to foster new partnerships between community and healthcare leaders to combat systemic racism and achieve a more just and equitable society."

## Statistics

| | *Total Cases* | *Total Deaths* | *Total Vaccine Doses Administered* |
|---|---|---|---|
| *Global* | 205,611,815 | 4,338,593 | 4,602,252,710 |
| *United States* | 36,307,177 | 619,094 | 352,842,072 |

JHU CSSE as of 1000 EDT 13 August 2021

| *Virginia* | Total cases (state) | Chesapeake | Hampton | Newport News | Norfolk | Portsmouth | Suffolk | Virginia Beach |
|---|---|---|---|---|---|---|---|---|
| Cases | 717,826 | 22,732 | 11,538 | 15,504 | 19,186 | 9,741 | 8,584 | 38,946 |
| Hospitalizations | 32,093 | 1,085 | 500 | 586 | 1,128 | 721 | 513 | 1,890 |
| Deaths | 11,599 | 311 | 184 | 244 | 278 | 206 | 195 | 425 |

VA DOH as of 1000 EDT 13 August 2021

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